

## FAST FACTS AND CONCEPTS #100 MEGESTROL ACETATE FOR CANCER ANOREXIA/CACHEXIA

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**Background** Cachexia occurs in up to 80% of cancer patients. Abnormal weight loss (more than 5-10% of pre-morbid weight) results in significant physical and psychological morbidity and is an independent risk factor for early mortality. Attempts to treat anorexia with enteral or parenteral feedings (see *Fast Fact #190*) have demonstrated limited efficacy, at the price of increased morbidity. This *Fast Fact* discusses megestrol acetate (MA), a synthetic progestin, as an appetite stimulant.

**Outcome Data** Overall, data suggests that approximately one in four patients taking MA will have an increase in their appetite, and one in twelve will have an increase in their weight. Clinical trials have also demonstrated that MA is:

- Equally efficacious to dexamethasone as an appetite stimulant.
- Associated with fewer long-term side effects than corticosteroids.
- Superior to dronabinol (see *Fast Fact #93*) in appetite stimulation and non-fluid weight gain.
- Effective when used concurrently with radiation therapy in lung or head and neck cancer to reduce treatment associated weight loss.

Despite these apparent benefits, most weight gain attributed from MA in clinical studies is largely adipose tissue and not lean muscle. Furthermore, no clear benefit to quality of life has been demonstrated, nor has any study shown a survival advantage from MA therapy.

**Dosing** The optimal timing to initiate treatment with MA (prophylactic or therapeutic) and the optimal duration of therapy are unknown. MA is typically dosed orally, once daily. There is an increasing dose/response curve from 160 to 800 mg/day; doses above 800 mg/day have no additional benefit. Different strategies include beginning at 400 mg per day and titrating for effect to 800 mg/day; or initiating treatment at 800 mg/day. Generally, MA is dosed in the elixir form both for patient convenience and cost (see below). MA is 60-80% excreted in urine; no guidelines are available for dosing in renal impairment.

**Costs** (AWP = average wholesale price)

- Tablet: 20 mg (AWP = \$69.20/100 pills); 40 tablets = 800 mg = \$27.68/day. 40 mg (AWP = \$123/100 pills); 20 tablets = 800 mg = \$24.60/day
- Elixir: 40 mg/ml (AWP = \$143.95/240 ml) = 20ml = 800 mg = \$11.90/day. 625 mg/5 ml (AWP = \$883.80/150 ml) = 5 ml = 625 mg = \$29.46/day.

**Adverse Effects** Multiple adverse effects have been reported including thromboembolic events (use with caution in patients with history thromboembolism), nausea, diarrhea, impotence, peripheral edema, hypertension, hyperglycemia, breakthrough uterine bleeding, and skin photosensitivity. MA can precipitate adrenal insufficiency via suppression of the hypothalamus-pituitary-adrenal axis.

**Future Considerations**

- Early investigational studies combining the use of MA with formoterol fumarate clinically significant improvement in muscle mass and/or function in cancer patients. More controlled trials are needed to determine if this combination is more effective than MA alone.
- Studies combining the use of carnitine and celecoxib suggest equal efficacy to using MA alone and may be an alternative for patients with contraindications to MA use.
- A recent clinical trial has suggested that the use of MA in children with cancer can be safe and associated with significant weight gain. However, more studies are needed to corroborate the safety and efficacy of pediatric MA therapy.

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